

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Decreasing referrals to Transient Ischemic Attack clinics during the COVID-19 outbreak. Results from a multi-centre cross-sectional survey.
AUTHORS	D'Anna, Lucio; Sheikh, Ambreen; Bathula, Raj; Elmamoun, Salwa; Oppong, Adelaide; Singh, Ravneeta; redwood, Rebecca; Janssen, John; Banerjee, Soma; vasilieiadis, evangelos

VERSION 1 – REVIEW

REVIEWER	Mor saban The Gertner Institute for Epidemiology and Health Policy Research, Ramat Gan; Israel
REVIEW RETURNED	06-Jul-2020

GENERAL COMMENTS	<p>Thank you for the opportunity to review this important manuscript. The article is well written and deals with a central issue during the covid-19 pandemic.</p> <p>Some specific comments:</p> <p>Introduction Line 15- please explain what is WSO? I would recommend thickening this section in general. For example, why there could be a decline? also suggest to describe a few numbers about the decline in ED referral during the pandemic (eg., Guglielmo et al., 2020; WongLaura et al., 2020; Saban et al., 2020).</p> <p>Method- I don't really understand why a survey was conducted (if u looking for TIA ED referral) and not a retrieval of data from the electronic medical record? Please explain</p> <p>Results- I would glad to see more statistical analyzes like patients clinical characteristics, arrival times, etc.</p> <p>Discussion- As i presented above there is already few studies focused on this issue, please refer</p>
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REVIEWER	Julie G Shulman Boston University Medical Center Boston, MA USA
REVIEW RETURNED	12-Jul-2020

GENERAL COMMENTS	<p>The authors present results of a survey sent to 5 stroke centers in their region to determine the number of patients referred to TIA clinics between March-April 2020 as compared to March-April 2019. The 100% response rate is impressive and the data is presented clearly, for the most part. A few points of clarification would help improve the strength of this paper.</p>
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	<p>Content comments:</p> <ul style="list-style-type: none"> - What specific questions did they survey ask? By what means did each individual stroke center determine the number of referrals? Were they asked to provide anonymized data supporting the numbers they gave in their survey responses? Is there any means of determining the accuracy of the numbers that each center reported? - Why do you think Hillingdon hospital saw an increase in referrals in March 2020 compared to March 2019, when the other 4 centers surveyed saw a decrease? How much did the referrals go up by? Would you consider this significant? Do you know the relative burden of COVID+ in that region/center compared to the others? Is there something unique about the patient population that seeks care at that center that would make their referral patterns different from the others? - The figure is nice but quite small and text is blurry, hard to read. Can this be made bigger and clearer? Would also clarify that the chart labeled "North West London region" is summarized data from the other 5 charts. That is not clear until after one has already read the paper carefully. You ideally want your figures to make sense to someone skimming. <p>Language/grammatical comments:</p> <ul style="list-style-type: none"> - Page 3, Strengths and Limitations: the first two bullets are poorly worded. Recommend rephrasing the first bullet, perhaps as: "This is the first study investigating the effects of COVID-19 on the volume of patients presenting to TIA clinics". It's unclear what point is being made with the second bullet ("...TIA clinical leads with insight...") -- would rephrase or remove. - Page 4, first sentence is a run-on. Would consider splitting into two, starting with, "Therefore, urgent assessment and management..." - Page 4 in methods, another run-on when listing the specific centers, gets confusing. Would consider splitting after the list ends: "...West Middlesex Hospital. Almost all stroke and TIA patients..." - Page 5, line 24: "...providing instructions for completion of the survey..." [manuscript currently says "competition" of the survey] - Page 6, line 52: Tenses are confusing. Consider changing to, "Out results highlight that patients, especially those with milder stroke symptoms, may have intentionally avoided hospitals..." - Page 7, line 8 – would change to "...as these more severe symptoms are less likely to be ignored by patients...". These definitely CAN be ignored! Just less likely. - Page 7, line 10 – would remove qualifier about "If I findings will be confirmed...". Whether your findings are confirmed or not, the remainder of the sentence is true – that patients and families need to be aware of early presentation even during challenging times.
REVIEWER	Houman Khosravani Division of Neurology, Department of Medicine, University of Toronto Sunnybrook Health Sciences Centre, Toronto, Canada
REVIEW RETURNED	13-Jul-2020
GENERAL COMMENTS	<p>The authors have reviewed referrals to transient ischemic attack (TIA) clinics in the COVID-19 era and have had a good response rate from the clinics surveyed within the Northwest London region - their findings demonstrate a significant decrease in referrals.</p> <p>This is an important study which highlights the change we are seeing globally with regards to TIA referrals. Some of the other</p>

	<p>findings in this disease including more complex and severe types of stroke such as large vessel occlusions, strokes due to overall coagulopathy, and endothilopathy likely exemplify a different mechanistic interaction between COVID-19 and stroke.</p> <p>The authors findings are important because they shed further light on, and further characterize, the decline in the presentations of minor stroke and TIA.</p> <p>One comment -can the authors please check, and add/write a brief paragraph stating that there have been no changes in the stroke systems/referral systems that would impact the referral patterns when comparing last year to this year, such that there are no confounders (within the limits of such a survey-based study), with regards to the effect being mostly due to COVID-19.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name

Mor saban

Institution and Country

The Gertner Institute for Epidemiology and Health Policy Research, Ramat Gan; Israel

Please state any competing interests or state ‘None declared’:

N/A

Please leave your comments for the authors below

Thank you for the opportunity to review this important manuscript.

The article is well written and deals with a central issue during the covid-19 pandemic.

Some specific comments:

Introduction

Line 15- please explain what is WSO?

We would like to thank the reviewer for their words of praise. We do apologise for not being very clear in line 15. WSO stands for World Stroke Organisation. For the benefit of the reviewer we added in the main text.

I would recommend thickening this section in general. For example, why there could be a decline? also suggest to describe a few numbers about the decline in ED referral during the pandemic (eg., Guglielmo et al., 2020; WongLaura et al., 2020; Saban et al., 2020).

We have expanded our introduction and taken into account the references suggested by the reviewer.

Method- I don't really understand why a survey was conducted (if u looking for TIA ED referral) and not a retrieval of data from the electronic medical record? Please explain.

We would like to thank the reviewer for having raised this important point. This survey provided a retrospective analysis on the number of patients reviewed in five different TIA clinics of the North West London region. We interviewed all the five TIA clinical leads that were asked to answer to our survey with the retrieval of data from their respective hospital archives. Unfortunately, as the five hospital do not belong to the same NHS Trust, we could not use a unique electronic archive to extract the data for all the centres involved in our analysis.

Results- I would glad to see more statistical analyzes like patients clinical characteristics, arrival times, etc.

We apologise but this analysis has not included the patient demographics and arrival times.

Discussion- As i presented above there is already few studies focused on this issue, please refer

We have taken into account the references suggested by the reviewer in the discussion.

Reviewer: 2

Reviewer Name

Julie G Shulman

Institution and Country

Boston University Medical Center

Boston, MA USA

Please state any competing interests or state 'None declared':

None declared

Please leave your comments for the authors below

The authors present results of a survey sent to 5 stroke centers in their region to determine the number of patients referred to TIA clinics between March-April 2020 as compared to March-April 2019. The 100% response rate is impressive and the data is presented clearly, for the most part. A few points of clarification would help improve the strength of this paper.

Content comments:

- What specific questions did they survey ask? By what means did each individual stroke center determine the number of referrals? Were they asked to provide anonymized data supporting the numbers they gave in their survey responses? Is there any means of determining the accuracy of the numbers that each center reported?

We would like to thank the reviewer for their words of praise and useful comments.

The survey was sent to all the five TIA clinical leads asked the following questions:

- What is the number of patients with suspected TIA referred to your TIA clinic service between 1st and 31st March 2019?
- What is the number of patients with suspected TIA referred to your TIA clinic service between 1st and 31st March 2020?
- What is the number of patients with suspected TIA referred to your TIA clinic service between 1st and 30th April 2019?
- What is the number of patients with suspected TIA referred to your TIA clinic service between 1st and 30th April 2020?

Each TIA clinical lead provided data on consecutive eligible patients referred to their service by using a databank of admissions that is used for reporting to a central UK stroke data bank Sentinel Stroke

National Audit Programme (SSNAP). Electronic and paper based medical records of eligible patients were retrieved from each hospital medical archive.

This survey was carried out using data collected as part of routine care and any researchers outside of the direct care team only had access to anonymised data.

- **Why do you think Hillingdon hospital saw an increase in referrals in March 2020 compared to March 2019, when the other 4 centers surveyed saw a decrease? How much did the referrals go up by? Would you consider this significant? Do you know the relative burden of COVID+ in that region/center compared to the others? Is there something unique about the patient population that seeks care at that center that would make their referral patterns different from the others?**

Many thanks for having raised this crucial point. As the lockdown actually started in UK only on the 23th March 2020, we compared the number of the referrals to the Hillingdon TIA clinic service between 23rd March to 30th April 2020, and between 23rd March to 30th April 2019. In the period between 1st and 22nd March 2020 the TIA clinic in Hillingdon received 21 consecutive referrals while only 11 in the same period of 2019 with an overall increase of 90.0%. On the other hand, as soon the lockdown started in UK (23rd March 2020) in the last week of March it has been documented a reduction of 50% in the number of the referrals compared to the same period of 2019. Moreover, as already documented in April 2020 compared to April 2019 it was a reduction in the number of referrals of 13.6%. Overall, considering the comparison between 23rd March to 30th April 2020, with the same period in 2019, the number of the referrals decreased by 19.23%.

	2019	2020	Difference %
1st -22nd March	11	21	+90.0%
23rd – 30th March	4	2	-50%

April	22	19	-13.6%
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As Hillingdon is part of the North West London region the population characteristics in terms of education and risk factors is similar to the other centre. Finally, we are not aware of any particular incidence of COVID-19 infection near Hillingdon during the period of time taken into consideration.

- **The figure is nice but quite small and text is blurry, hard to read. Can this be made bigger and clearer? Would also clarify that the chart labeled “North West London region” is summarized data from the other 5 charts. That is not clear until after one has already read the paper carefully. You ideally want your figures to make sense to someone skimming.**

Many thanks for this important suggestion. To make the figure more readable we changed and added a new Table.

Language/grammatical comments:

- **Page 3, Strengths and Limitations: the first two bullets are poorly worded. Recommend rephrasing the first bullet, perhaps as: “This is the first study investigating the effects of COVID-19 on the volume of patients presenting to TIA clinics”. It’s unclear what point is being made with the second bullet (“...TIA clinical leads with insight...”) -- would rephrase or remove.**
- **Page 4, first sentence is a run-on. Would consider splitting into two, starting with, “Therefore, urgent assessment and management...”**
- **Page 4 in methods, another run-on when listing the specific centers, gets confusing. Would consider splitting after the list ends: “...West Middlesex Hospital. Almost all stroke and TIA patients...”**
- **Page 5, line 24: “...providing instructions for completion of the survey...” [manuscript currently says “competition” of the survey]**
- **Page 6, line 52: Tenses are confusing. Consider changing to, “Our results highlight that patients, especially those with milder stroke symptoms, may have intentionally avoided hospitals...”**

- Page 7, line 8 – would change to “...as these more severe symptoms are less likely to be ignored by patients...”. These definitely CAN be ignored! Just less likely.
- Page 7, line 10 – would remove qualifier about “If I findings will be confirmed...”. Whether your findings are confirmed or not, the remainder of the sentence is true – that patients and families need to be aware of early presentation even during challenging times.

All the language/grammatical comments have been acknowledged in the main text.

Reviewer: 3

Reviewer Name

Houman Khosravani

Institution and Country

Division of Neurology, Department of Medicine, University of Toronto Sunnybrook Health Sciences Centre, Toronto, Canada

Please state any competing interests or state ‘None declared’:

None

Please leave your comments for the authors below

The authors have reviewed referrals to transient ischemic attack (TIA) clinics in the COVID-19 era and have had a good response rate from the clinics surveyed within the Northwest London region - their findings demonstrate a significant decrease in referrals.

This is an important study which highlights the change we are seeing globally with regards to TIA referrals. Some of the other findings in this disease including more complex and severe types of stroke such as large vessel occlusions, strokes due to overall coagulopathy, and endothilopathy likely exemplify a different mechanistic interaction between COVID-19 and stroke.

The authors findings are important because they shed further light on, and further characterize, the decline in the presentations of minor stroke and TIA.

One comment -can the authors please check, and add/write a brief paragraph stating that there have been no changes in the stroke systems/referral systems that would impact the referral patterns when comparing last year to this year, such that there are no confounders (within the limits of such a survey-based study), with regards to the effect being mostly due to COVID-19.

We would like to thank the reviewer for their words of praise and useful comments. We added the statement in the main text as suggested.

VERSION 2 – REVIEW

REVIEWER	Julie Shulman Boston Medical Center Boston, MA USA
REVIEW RETURNED	23-Aug-2020
GENERAL COMMENTS	While the authors addressed the language and grammatical comments included in the initial review of this paper, they did not address any of the content concerns raised with the initial review. These are the more significant of the initial review comments and should be addressed, either with a change in the manuscript or

	<p>commentary on why the authors are choosing to not change the manuscript. A "response to reviewer" letter would be helpful if the authors choose the latter approach.</p> <p>Copied from the original review, still applicable to this version:</p> <ul style="list-style-type: none"> - What specific questions did the survey ask? By what means did each individual stroke center determine the number of referrals? Were they asked to provide anonymized data supporting the numbers they gave in their survey responses? Is there any means of determining the accuracy of the numbers that each center reported? - Why do you think Hillingdon hospital saw an increase in referrals in March 2020 compared to March 2019, when the other 4 centers surveyed saw a decrease? How much did the referrals go up by? Would you consider this significant? Do you know the relative burden of COVID+ in that region/center compared to the others? Is there something unique about the patient population that seeks care at that center that would make their referral patterns different from the others? - The figure is nice but quite small and text is blurry, hard to read. Can this be made bigger and clearer? Would also clarify that the chart labeled "North West London region" is summarized data from the other 5 charts. That is not clear until after one has already read the paper carefully. You ideally want your figures to make sense to someone skimming.
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Reviewer Name

Julie G Shulman

Institution and Country

Boston University Medical Center

Boston, MA USA

Please state any competing interests or state 'None declared':

None declared

Please leave your comments for the authors below

While the authors addressed the language and grammatical comments included in the initial review of this paper, they did not address any of the content concerns raised with the initial review. These are the more significant of the initial review comments and should be addressed, either with a change in the manuscript or commentary on why the authors are choosing to not change the manuscript. A "response to reviewer" letter would be helpful if the

authors choose the latter approach.

We would like to thank again the reviewer for their words of praise and very useful comments. Our response to the reviewer's points was already included in our last re-submission. We added our response below for the reviewer's benefit and we modified the main manuscript accordingly.

Copied from the original review, still applicable to this version:

- What specific questions did the survey ask? By what means did each individual stroke center determine the number of referrals? Were they asked to provide anonymized data supporting the numbers they gave in their survey responses? Is there any means of determining the accuracy of the numbers that each center reported?

The survey was sent to all the five TIA clinical leads asked the following questions:

- What is the number of patients with suspected TIA referred to your TIA clinic service between 1st and 31st March 2019?
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Each TIA clinical lead provided data on consecutive eligible patients referred to their service by using a databank of admissions that is used for reporting to a central UK stroke data bank Sentinel Stroke National Audit Programme (SSNAP). Electronic and paper based medical records of eligible patients were retrieved from each hospital medical archive.

This survey was carried out using data collected as part of routine care and any researchers outside of the direct care team only had access to anonymised data.

- Why do you think Hillingdon hospital saw an increase in referrals in March 2020 compared

to March 2019, when the other 4 centers surveyed saw a decrease? How much did the referrals go up by? Would you consider this significant? Do you know the relative burden of COVID+ in that region/center compared to the others? Is there something unique about the patient population that seeks care at that center that would make their referral patterns different from the others?

Many thanks for having raised this crucial point. As the lockdown actually started in UK only on the 23th March 2020, we compared the number of the referrals to the Hillingdon TIA clinic service between 23rd March to 30th April 2020, and between 23rd March to 30th April 2019. In the period between 1st and 22nd March 2020 the TIA clinic in Hillingdon received 21 consecutive referrals while only 11 in the same period of 2019 with an overall increase of 90.0%. On the other hand, as soon the lockdown started in UK (23rd March 2020) in the last week of March it has been documented a reduction of 50% in the number of the referrals compared to the same period of 2019. Moreover, as already documented in April 2020 compared to April 2019 it was a reduction in the number of referrals of 13.6%. Overall, considering the comparison between 23rd March to 30th April 2020, with the same period in 2019, the number of the referrals decreased by 19.23%.

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As Hillingdon is part of the North West London region the population characteristics in terms of education and risk factors is similar to the other centre. Finally, we are not aware of any particular incidence of COVID-19 infection near Hillingdon during the period of time taken into consideration.

- The figure is nice but quite small and text is blurry, hard to read. Can this be made bigger and clearer? Would also clarify that the chart labeled “North West London region” is summarized data from the other 5 charts. That is not clear until after one has already read the paper carefully. You ideally want your figures to make sense to someone skimming.

Many thanks for this important suggestion. To make the figure more readable we changed the figure and added a new Table.

VERSION 3 – REVIEW

REVIEWER	Julie Shulman Boston University Medical Center USA
REVIEW RETURNED	29-Sep-2020
GENERAL COMMENTS	Comments from previous revisions were adequately addressed. No further comments.